Remarks/Arguments

Prior to the present amendments, claims 38-46 were pending in this application. Claims 38, 39, 41, 43, and 46 have been amended and claims 42, 44 and 45 have been canceled. All amendments are supported by the specification as originally filed and do not add new matter. Specific support for the amendments is at least in original claim 5, paragraphs [0034] and [0035] and paragraph [0100] of the specification as published under publication no. 20040087774. The amendments and cancellations were made without prejudice or disclaimer. Applicants explicitly reserve the right to pursue any deleted subject matter in one or more continuing applications.

Election/Restrictions

Applicant note the finality of the restriction requirement.

Priority

Applicants note and appreciate the acknowledgement of the priority claim for this application.

Information Disclosure Statement

Applicants note and appreciate the consideration of the information disclosure statements submitted on April 19, 2004 and April 19, 2005.

Claim Rejections – 35 USC §112

(1) Claim 46 has been rejected under 35 USC 112, second paragraph, as allegedly being indefinite for its recitation of the phrase "Epstein-Barr virus associated tumor cell." Since the phrase is not longer present in the claim, the present rejection is believed to be moot.

(2) Claims 38-46 were rejected under 35 USC 112, first paragraph as allegedly failing to comply with the written description requirement. According to the rejection, the specification does not provide an adequate written description for (i) polypeptides having 70%

sequence identity with the TRAF binding domain of native I-TRAF, (ii) fragments of native I-TRAF and fragments of I-TRAF polypeptides having 70% sequence identity with the TRAF binding domain of native I-TRAF polypeptide,(iii) the truncated murine I-TRAF-alpha polypeptide, (iv) the equivalent part of a human I-TRAF sequence, (v) the TRAF2 binding fragments, (vi) polypeptides having at least 70% sequence identity with SEQ ID NO: 5, and (vii) the conditions suitable for expression of the I-TRAF polypeptide from the nucleic acid molecule.

Claims 42, 44 and 45 have been canceled. The rejection of the remaining claims is respectfully traversed.

Without acquiescence to the rejection, the claims have been amended to recite a 90% instead of a 70% sequence identity and to remove a reference to the TRAF binding domain of native I-TRAF with regard to sequence identity. In addition, the claims have been amended by reciting that the nucleic acid molecules inhibit a TRAF-mediated signaling event. Applicants submit that a high degree of sequence identity coupled with a clear functional recitation satisfies the written description prong of 35 USC 112, first paragraph.

As far as the Examiner's comments on the "conditions suitable for expression of the I-TRAF polypeptide" are concerned, Applicants submit that the specification of a patent application is directed to a person of ordinary skill in the pertinent art. Since there is no indication in the specification that the expression of an I-TRAF polypeptide would require any specific, unique conditions, a person of ordinary skill, reading the disclosure of the present application would clearly understand that I-TRAF can be expressed under conditions well known for the expression of recombinant proteins is various recombinant host cells, such as, for example, the conditions described on pages 22-23 of the specification and the referenced textbooks.

It is further submitted that the specification clearly explains the properties deemed to be important for inhibiting the TRAF-mediated signaling. Thus, for example, at page 9, lines 9-19, the specification explains that such molecules, referred to as "functional derivatives," are defined by their ability "to inhibit the association of member of the TNF receptor superfamily with which the TRAF is naturally associated, with the proviso that such functional derivatives are not (anti-TRAF or anti-TNF receptor superfamily member) blocking antibodies. Preferably, a functional derivative binds to a native TRAF polypeptide, such as TRAF 1, TRAF2 and/or TRAF3 thereby (reversibly or irreversibly) preventing its interaction with cell surface receptors (e.g., TNF-R2, CD40, CD30) that trigger TRAF-mediated NF-.kappa.B activation cascades. In a particularly preferred embodiment, the prevention of TRAF-mediated signaling is reversible, and the TRAFs can be released from their latent, inhibited state, e.g. by ligand-mediated receptor aggregation."

In view of this explanation, one of ordinary skill would reasonably conclude that applicants were in the possession of the invention as currently claimed, and therefore, the present rejection should be withdrawn.

(3) Claims 38-46 were rejected under 35 U.S.C. 112, first paragraph as allegedly failing to comply with the enablement requirement. In support of the rejection, the Examiner notes that the specification does not provide adequate enablement for (i) *in vivo* modulation of TRAF-mediated signal transduction; (ii) *in vitro* and *in vivo* methods comprising introducing into a cell a large genus of polypeptides that encompass fragments and truncations of I-TRAF; (iii) *in vitro* and *in vivo* methods of modulating TRAF mediated signal transduction comprising introducing into a cell a large genus of polypeptide that encompass fragments and truncations of I-TRAF, and (iv) the methods of modulating TRAF mediated signal transduction in all known cells. (Office Action, page 6)

Without acquiescence to the rejection, the claims now recite "inhibition" instead of "modulation," therefore the Examiner's comments in this regard are moot.

In addition, the claims now recite cancer cells that express TRAF, and an at least 90% sequence identity to native sequence polypeptides. Thus, one of ordinary skill could clearly practice these aspects of the invention without undue experimentation. Applicants specifically disagree with the examiner's comment that "the skilled artisan would require to conduct an undue amount of experimentation to practice the present method using all available cells that do express TRAF molecule." (Page 9, first full paragraph) It is noted that a significant amount of experimentation is allowed, if the experimentation is merely routine. In the present case, detecting the present of TRAF nucleic acid or the encoded protein in a cell might require time, but can be performed by methods that were routine in the art at the time the present invention was made. Therefore, identification of TRAF-expressing cells, especially TRAF-expressing cancer cells does not require undue experimentation.

Applicants also disagree with the Examiner's assertion that the in vitro data provided in the specification do not enable the in vivo use of the claimed methods. As the Examiner has acknowledged in other parts of the Office Action, the specification clearly explains the mechanism of action for I-TRAF, in particular the interaction of TRAF and I-TRAF. Thus, there is no reason why the in vitro data would not translate into an in vivo setting.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

In conclusion, all claims pending in this application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account 07-1700 (Attorney Docket No. 39766-0255D1C3).

Respectfully submitted,

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Ginger R. Dreger, Esq.
Reg. No. 33,055

GOODWIN PROCTER LLP
Customer No. 77845
181 Lytton Avenue
Palo Alto, CA 94301
Tel: (650) 752-3100
Fax: (650) 853-1038